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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/060,609	04/15/98	OZENBERGER	B	AHP98126

HM12/0323

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EXAMINER	
DUFFY, P	
ART UNIT	**PAPER NUMBER**
1645	11

DATE MAILED: 03/23/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/060,609	Ozenberger et al.
Examiner	**Group Art Unit**
DUFFY	1645

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on Nov. 18, 1999.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1 - 24 is/are pending in the application.

Of the above claim(s) 6-10, 12-24 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-5 and 11 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☑ Claim(s) 1-24 are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4

☐ Interview Summary, PTO-413

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☒ Other Notice to comply with Sequence Rules

Office Action Summary

DETAILED ACTION

Sequence Requirements

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicants have disclosed multiple nucleic acid sequences on pages 22-27, none of which comply with the sequence rules. Full compliance with the sequence rules is required in response to this office action.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

3. This application has been filed with formal drawings which are acceptable for examination purposes only. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152.

Correction of the noted defects in the drawings can be deferred until the application is allowed by the examiner.

Election/Restriction

4. Applicant's election of Group I, claims 1-5 and 11 in Paper No. 8, mailed November 18, 1999 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

5. Claims 6-10 and 12-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8, mailed November 18, 1999.

Double Patenting

6. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

7. Claims 1-5 and 11 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim s 1-5 and 11 of copending Application No. 09/172,990. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Specification

8. The title and abstract of the invention are not descriptive. A new and abstract title are required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

9. Claims 1-5 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

As to claim 1, Markush members (j -allelic variant), (k-species homologs), and (l-hybridizing nucleic acids), the specification broadly describes as part of the invention isolated polynucleotides comprising the novel isolated polynucleotides which encode gene products that selectively bind human β-amyloid ("BBP", see page 2, lines 19-20). The specification also broadly describes their novel "BBP" specifically by a novel reference polynucleotide sequence of SEQ ID NO:1 which is the cDNA sequence encoding the BBP protein of SEQ ID NO:2. It is evident from these pages of the specification that applicant is describing their novel BBP gene product specifically by a novel reference cDNA polynucleotide sequence (SEQ ID NO:1) and generically by and reference to a polynucleotide sequence encoding the novel polypeptide sequence (SEQ ID NO:2). The specification broadly contemplates polynucleotides comprising the

gene corresponding to the cDNA sequence of SEQ ID NO:1 and species homologs of SEQ ID NO:1 or SEQ ID NO:2. Applicants also broadly describe the invention as embracing any substitution, insertion or deletion change of nucleotides throughout the entire stretch of nucleotides found in the reference sequence by use of hybridizing language. Applicants also contemplate alleles of a gene. A gene is defined in the art to specifically include continuous or discontinuous regions encoding the polypeptide and may also contain additional coding and non coding regions (see definition of gene in "GENES IV" by Lewin, B., page 810). Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). As depending from these are the vectors, host cells and methods of producing the polypeptide. The claims encompass polynucleotide sequences that have a unrecited degree of change as compared to a reference nucleic acid sequence comprising SEQ ID NO:1 (i.e. the hybridizing language), genes, alleles, homologues which correspond to sequences from other species, genes, mutated sequences and allelic variants. None of these sequences meets the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

The specification only discloses a polynucleotide sequence comprising SEQ ID NO: 1 which corresponds to the polynucleic acid sequence encoding the species of the protein "BBP" which is a amyloid binding protein comprising SEQ ID NO:2. An isolated polynucleotide comprising a nucleotide sequence encoding SEQ ID NO:2, is also described by way of the written description in view of the art established principle of wobble variants of triplet codons for particular bacterial amino acids as described in basic textbooks. Thus, an isolated polynucleotide sequence comprising SEQ ID NO: 1 (and specifically recited fragments thereof) and an isolated polynu otide comprising of a nucleotide sequence encoding SEQ ID NO:2 (and specifically recited fra nts thereof) meet the written description provision of 35 USC 112, first paragraph.

Applicants hav scribed nor disclosed the gene encoding SEQ ID NO:1 or SEQ ID. NO:2, a species homologs c variants which encode the "BBP" gene. A functional gene encompasses much more ein coding region (see Lewin et al, GENES IV, page 810). A mammalian gene is con ssociated with positive and negative controlling elements such as promoters and enl l is characterized by introns and exons, without which, no protein is expressed. The s n fails to describe the gene *per se* (i.e., the nucleic acid gene which encodes SEQ nd which applicants have intended to be encompassed by the comprising and encoding lang e instant claims as set forth *supra*. There is no known or disclosed correlation betw unction and the structure of the non-described regulatory elements and untranslated regions of the genes. Furthermore, there is no additional disclosure of physical and/or chemical properties which define the gene or the genus of species homologs. In a mammalian genome, the recitation of a gene encoding SEQ ID NO:2 or comprising SEQ ID NO:1, includes regulatory sequences which are essential to the operation

and function of the gene. These regulatory and other gene sequences of the gene that are not described, are essential to the function of the structural BBP gene and are therefore essential elements. Such sequences fail to have an adequate written description in the instant specification. The specification does not provide written description support for any controlling flanking nucleic acid sequences or introns which such that conception and possession of the gene encoding SEQ ID NO:2 is present in the specification as originally filed. The specification does not provide any polynucleotide structure for a significant fragment or gene segment or allelic variant of the BBP gene, a cDNA or gene sequence of the polynucleotide sequence of any species homologs, or sequences which hybridize to SEQ ID NO:1 which are not fully complementary. Since, the skilled artisan would expect substantial variation between genes, alleles, species homologs and hybridizing nucleic acids it is apparent to one having skill in the art that applicants were not in possession of the claimed invention at the time of filing. With the exception of an isolated polynucleotide comprising SEQ ID NO: 1 and an isolated polynucleotide encoding the polypeptide sequence of SEQ ID NO:2, the skilled artisan cannot envision all the contemplated nucleotide sequences by the detailed chemical structure of the claimed polynucleotides and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Therefore, only an isolated

polynucleotide comprising of SEQ ID NO: 1 and an isolated polynucleotide encoding SEQ. ID NO:2, and specifically claimed fragments of SEQ ID NO:1 and corresponding fragments of SEQ ID NO:2, but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

10. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide comprising SEQ ID NO:1 an isolated polynucleotide encoding SEQ ID NO:2, vectors comprising these nucleic acids, host cells comprising the vectors, the specification does not reasonably provide enablement for genes, species homologs and allelic variants of SEQ ID NO:1 or SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As to claims 1-5, the claims are drawn to and encompass polynucleotides which are genes species homologs and allelic variants of SEQ ID NO:1 or comprise a nucleotide sequence which has a recited percent identity or average variability as compared to a sequence comprising SEQ ID NO:1 and vectors and host cells and methods of using the host cell to produce the protein comprising these polynucleotides. These claims are not enabled for the following reasons. The written description is limited to SEQ ID NO:2 which is the corresponding amino acid sequence encoded by the polynucleotide consisting of SEQ ID NO:1. The specification fails to indicate that SEQ ID NO:2 has the biological activity of a human amyloid binding protein and

lacks any description of any variants of a SEQ ID NO:1 which act as a human amyloid binding protein. The specification is not enabled for any variants of a polynucleotide comprising SEQ ID NO:1 or SEQ ID NO:2, the specification fails to teach what are the critical nucleic acid and protein residues that can be modified to change the amino acid structure of SEQ ID NO:2 and still achieve a nucleic acid encoding a protein with similar functional (i.e., amyloid binding activity) One of skill in the art would be reduced to merely randomly altering nucleic acids and amino acid(s) which would lead to unpredictable results regarding the functional activity of the protein and the ability of the nucleic acid to be an amyloid binding protein. Protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted a *priori* and must be determined empirically on a case by case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3):1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. The specification has not conceived any other functionally equivalent protein variant or

the polynucleic acid sequence encoding the protein variant does not set forth the general tolerance to substitutions and where substitutions could be made. The specification fails to teach any species homologs or allelic variants. Since, the specification lacks a written description of any variants, genes, alleles or species homologs, it is not enabled for this language because it fails to enable the skilled artisan to envision the detailed chemical structure of the claimed polynucleotide encoding protein variants of SEQ ID NO:2 respectively, as well as the screening method of obtaining them, as well as how to use the polynucleotides encoding the protein variants, one of skill in the art would be unable to produce these polynucleotides encoding protein variants or polynucleotide variants encompassed by the instant claims. It is noted that Markush members of (b), (c), (e) and (f) require the use of specifically deposited clones. Applicant's referral to the deposit of these clones at the ATCC in the specification is an insufficient assurance that all required deposits have been made and all the conditions of 37 CFR §1.801-1.809 have been met. If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty *and* that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application. These requirements are necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. *Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required.*

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;
3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;
6) The procedures used to obtain a sample if the test is not done by the depository; and
7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the hybridoma cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed. Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice. .

In view of the lack of written description of any protein variant or species homolog that functions equivalently to the protein of SEQ ID NO:2 and the corresponding nucleic acid sequence, the lack of written description of the gene comprising SEQ ID NO:1 or any alleles therefore, the lack of enabling description of make and use polynucleotides encoding protein variants of SEQ ID NO:2, the lack of an enabling written description of how to obtain and make and use the nucleic acid variants of the of the amino acid of SEQ ID NO:2, the unpredictability associated with making and using the nucleic acids encoding the myriad variants of SEQ ID NO:2 encompassed in the scope of the claims as set forth above, the lack of teaching even a beginning point for variation of the nucleic acid corresponding to a variant of the protein sequence of SEQ ID NO:2 for routine experimentation, lack of working examples commensurate in scope with the instant claims, the skilled artisan would be forced into undue experimentation to practice (i.e. make and use) the invention as is broadly claimed.

11. Claims 11 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to oligonucleotides which are complementary to a portion of SEQ ID NO:1 and which inhibit expression of the BBP1 gene. The specification fails to teach any use at all. The specification fails to describe any *in vitro* or any *in vivo* use for this claimed product. The specification has no apparent description of how to make and use these antisense oligonucleotides. Applicants are invited to point to the page and line number in the specification where written description can be found for how to make and use these oligonucleotides. While the courts have that a patent need not teach, and preferably omits, what is well known in the art. The omission of all details of how to make and use the product can not constitute an enabling specification. Reliance on the skill of the art would not be persuasive to remove this rejection because; as also recognized by the Federal Circuit:

> "However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material *or of any conditions under which a process can be carried out,* [emphasis added] undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research." (Genentech Inc. v. Novo Nordisk A/S Ltd., 42 USPQ2d 1001).

In the instant case there is no disclosure of any conditions under which the process of inhibition can be carried out or how to assay for such inhibition. The specification is apparently devoid of

any description of how to make and use such oligonucleotides. As such, the failure of this specification of how to make and use the oligonucleotides constitutes undue experimentation.

12. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "An oligonucleotide which encodes an antisense sequence "complementary" to a portion of BBP1 sequence of SEQ ID NO:1.. "is confusing because by definition an antisense sequence is "complementary" to SEQ ID NO:1. The examiner suggests that one of the following would obviate this rejection. " An oligonucleotide which is complementary to a portion of BBP1 sequence of SEQ ID NO:1 and which inhibits an expression of the BBP1 gene." or "An oligonucleotide which encodes an antisense sequence which is complementary to a portion of BBP1 sequence of SEQ ID NO:1 and which inhibits expression of the BBP1 gene."

Claim Rejections - 35 USC § 102 or 103

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

15. Claim 1 and 11 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by EST178050, Accession number AA306979 (Adams et al Nature, 377 (6547, Suppl), 3-174, 1995).

Adams et al teach a polynucleotide which is 54.9% identical to SEQ ID NO:1 of the instant application (see attached alignment). Adams et al teach the sequence in a pBluescript SK- vector. The complementary strand is instantly appreciated in view of the disclosure of the coding strand. Moreover, the recitation of "stringent conditions" is inclusive of very low stringency conditions which would not exclude the polynucleotide sequence of SEQ ID NO:1. Moreover, because the local similarity is so high the sequence or portion thereof would hybridize and inhibit the expression of BBP1, absent convincing factual evidence to the contrary.

16. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over EST178050, Accession number AA306979 (Adams et al Nature, 377 (6547, Suppl), 3-174, 1995) in view of Sambrook et al (Molecular Cloning, 1989, Cold Spring Harbor Laboratory Press, pp17.1-17.44).

EST178050, Accession number AA306979 (Adams et al Nature, 377 (6547, Suppl), 3-174, 1995) is set forth supra. The reference does not teach an expression vector, in a host cell and recovery of the protein of interest.

Sambrook et al teach the desirability of expression of cloned gene in *Escherichia coli*. Sambrook et al teach the placement of the DNA of interest in an expression vector which comprises an expression control sequence operably linked to the DNA of interest, introduction of the expression vector into *Escherichia coli* and expression and purification of the expressed protein using a variety of techniques.

It would have been prima facie obvious to one having ordinary skill in the art a the time the invention was made to express the polypeptide encoded by the nucleic acid of Adams et al by subcloning into an expression vector and placing the vector in a compatible host cell and incubating the host cell under appropriate conditions using the expression system of Sambrook et al, because Sambrook et al teach that expression of large amounts of protein from a cloned gene introduced into *Escherichia coli* has proven invaluable in the study of the characterization, localization and functional analysis of proteins.

Status of Claims

17. No claims are allowed.

18. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995.

Patricia A. Duffy, Ph.D.
March 17, 2000

Patricia A. Duffy

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600

Application No.: 09/060,609

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: see office Action

Applicant Must Provide:

☒ An ~~initial or~~ substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An ~~initial~~ or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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